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ABSTRACT

Xavier University (XU) and the Tulane Cancer Center (TCC) will build a core of human talent that will address scientific problems such as drug resistance and the effect of environmental agents on breast cancer (BC) in the African-American community. A multi-part research and training program will generate data, develop new research programs and train new faculty and African-American students in BC research. The first component will fund two research projects. The Wang and Burow project will elucidate a previously unexplored cellular signaling mechanism that leads to drug resistance in breast carcinoma cells derived from African American women and women of other ethnicities. The Wiese and Hill project will identify and characterize the genes and gene products associated with BC cell proliferation induced by exposure to pesticide mixtures and is relevant to the African American community in Southern States where pesticide exposure is relatively high. The second part of the program aims to increase the number of faculty at XU involved in BC research by supporting two junior faculty members to develop BC research projects with a TCC mentor. The third objective will support research training of XU undergraduates and pharmacy students. The fourth objective will provide workshops, seminars and research opportunities in BC research for the XU community. This program will enhance the understanding of unique aspects of BC development and progression among African American women and will contribute to the elimination of the "mortality gap" between African-American BC patients and women of other ethnicities.

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Introduction

African American women are at higher risk for breast cancer (BC) mortality compared with their white counterparts. Over the past decade BC mortality has decreased 1%-2% per year in white women, but not in African-American women. The resulting "mortality gap" is a serious national problem, and understanding the reasons for it and developing solutions must be a high priority. Thus, BC research must focus on developing breast cancer models that would aim to accurately predict the disease development and progression among African-American women. ***We are convinced that increasing the involvement of African American students in BC research will greatly contribute to increasing awareness of the disease in the African American community, which in turn will increase the likelihood of early detection of the disease. Furthermore, the focus on the unique aspects of BC in African American women will lead to better understanding of the disease, and to better treatment options for African American women. This will eventually minimize or eliminate the BC "mortality gap".*** To this end we are developing a training program at Xavier University of Louisiana (XU) in collaboration with the Tulane University Cancer Center (TCC). More than 90% of Xavier's student body is African American has active programs (MBRS, MARC, RISE, NSF/MIE) designed to increase the number of minority students pursuing careers in medical and biomedical research. Through this BC training program, African American students will have the opportunity to become involved in BC research. Tulane (TU) and Xavier have a long history of collaborations involving joint centers and programs and individual collaborations between Tulane and Xavier faculty and staff are common. This new initiative will provide funds for yet another collaboration offering a unique opportunity for XU researchers to establish a BC research program for the benefit of XU students and, eventually, the African-American community. The goals of the training program are to create an environment that fosters BC research, in which XU investigators will receive substantive training and to complete substantive research projects of high relevance to the eradication of BC. The program will enable XU investigators to publish their results in peer-reviewed literature and advance toward independently funded BC research programs. The program includes two full research projects that involve an XU researcher and a qualified TCC mentor. The program will identify two additional XU researchers who have expressed an interest in BC research but do not have prior funding in BC. Participating XU faculty will get the opportunity to network and learn about BC research through participation in the TCC weekly seminar program and the signal transduction workshop that will focus on breast and prostate cancer. The two additional XU faculty involved will develop a mini-proposal in Y1-2 and carry out pilot studies with the advisory of a mentor faculty from TCC in Y2-4. The results of all program research studies will be used as a basis for future proposals in the area of BC. Yearly symposia will be held to provide information to XU students and faculty as well as to enrich the experience of the participating members regarding research opportunities in BC. Multiple project group meetings will be held each year to discuss current data, manuscripts in preparation, funding opportunities and issues regarding project operations.

Body

<u>Task 1</u>

Complete two substantive research projects of high relevance to eradication of breast cancer

Project 1

Chemoresistance in Breast Carcinoma Cells: MEK5-BMK/Erk5 Expression and Proteomic Analyses"

Guangdi Wang, Ph.D., Department of Chemistry, Xavier University of Louisiana PI (Trainee)
Mathew E. Burow, Ph.D., Department of Medicine, Tulane University School of Medicine (Mentor)

Aim 1: To demonstrate the requirement for and the role of the MEK5 pathway in survival signaling and suppression of apoptosis in MCF-7 breast carcinoma cells.

(1). Implicate MEK5 activation in cell survival signaling, prevention of anti-estrogen and chemotherapeutic drug-induced cell death using MCF-7 stable, transiently transfected cells and ZR-75-30. (Months 1-18).

(2). Implicate apoptotic suppression as a mechanism for MEK5-mediated survival and drug-resistance (Months 12-24).

Year One Progress

We have characterized the effects of MEK5-Erk5 on cell survival signaling using the MCF-7 cell line. These initial studies will allow use to proceed with our proposed studies in Aim#2 involving the proteomic characterization of MEK5-Erk5 signaling in MCF-7 cells. Additionally using this system we have established that expression/activation of the MEK5-Erk5 pathways promoters enhanced tumor growth/formation and progression to hormone-independence of in vivo breast tumors in immunocompromised mice. Using a SCID model of *in vivo* tumorigenesis we demonstrate that MEK5 expressing cells possessed an early tumor onset and greater tumor growth than VEC cells (**Figure 1**). Of significant interest was the observation that the MEK5 cells were capable of tumor formation in the absence of exogenous estrogen while the ER-positive VEC parent MCF-7 cells were unable to form tumors without estrogen, demonstrating MEK5's role in progression to a more malignant hormone-independent phenotype. What is interesting about this data is the potentiation of both tumor size and early onset when MEK5 and estrogen are combined. At some levels this suggests that these two pathways regulate distinct components of a cancer cells proliferation and survival/apoptotic cascades. Additionally, the ability of MEK5 to lead to both an anti-estrogen resistant phenotype *in vitro* and a hormone-independent phenotype *in vivo* in many ways parallels what is observed in advanced/recurrent ER+ breast carcinoma's progression to therapeutic resistance..

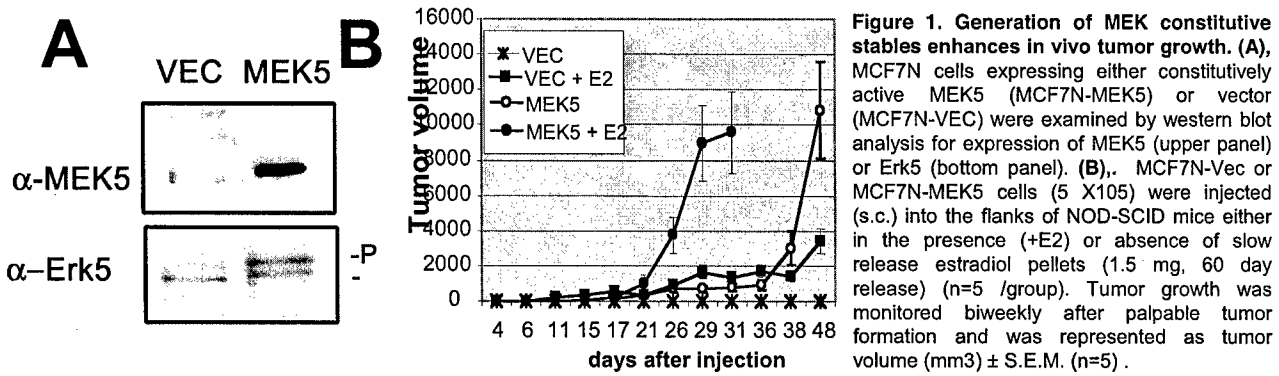

Figure 1. Generation of MEK constitutive stables enhances in vivo tumor growth. (A), MCF7N cells expressing either constitutively active MEK5 (MCF7N-MEK5) or vector (MCF7N-VEC) were examined by western blot analysis for expression of MEK5 (upper panel) or Erk5 (bottom panel). **(B),**. MCF7N-Vec or MCF7N-MEK5 cells (5 X105) were injected (s.c.) into the flanks of NOD-SCID mice either in the presence (+E2) or absence of slow release estradiol pellets (1.5 mg, 60 day release) (n=5 /group). Tumor growth was monitored biweekly after palpable tumor formation and was represented as tumor volume (mm3) ± S.E.M. (n=5) .

Aim 2: To characterize differences in protein expression between MCF-7N (APOP-Sensitive), MCF-7M (APOP-Resistant) and ZR-75-30 breast carcinoma cells and identify anti-apoptotic proteins, such as Survivin, within MEK5-expressing cell lines.

(1) Prepare samples for 2D gel separation. (Months 18-24).
(2) Separate proteins on 2D gel electrophoresis, compare differences in protein expression, and perform in-gel tryptic digestion of excised protein products. (Months 24-36).
(3) Sequences obtained from tryptic digests will be used to characterize and identified protein expression differences between drug resistant ZR-75-30 and MCF-7 breast carcinoma cells with a focus on known anti-apoptotic proteins or novel apoptotic domain containing proteins (BCl-2 homology (BH), baculovirus IAP repeat (BIR0, caspase activation recruitment domain (CARD), etc.). (Months 24-36).

Year One Progress

Hired Research Associate

Mr. Qiang Zhang has been hired as a research associate to work full time on the breast cancer project. Mr. Zhang has extensive experience in mass spectrometry and a variety of separation techniques that are essential to the success of the project. Mr. Zhang started working on the project in August of 2004.

Collaboration between Dr. Burow at Tulane Cancer Center and Dr. Wang

Through frequent phone, email, and personal contact, a close collaborative relationship has been established between Dr. Matthew Burow's research group at TCC and Dr. Guangdi Wang's lab at Xavier University. Dr. Burow's lab has provided cultures of two breast cancer cell lines for Dr. Wang's lab to conduct initial

experiments involving 1) method development and optimization for 2D gel separation of proteins, imaging and spot selection for digestion, and HPLC-tandem mass spectrometry (MS/MS) for protein identification; and 2) overall comparison of proteomes of the two cell lines. The two cell lines that are currently being analyzed by 2D gel and HPLC-MS/MS are the MEK5 expressing breast carcinoma cell (MCF-7M-MEK5) and the drug sensitive MCF-7N-VEC cell line.

Collaboration between the Proteomic Lab at the Children's Hospital in New Orleans and Dr. Wang's Lab

The fact that neither Dr. Burow's lab at TCC nor Dr. Wang's lab at Xavier is equipped with a complete line of proteomic analysis instruments, it is necessary that we seek long-term collaboration with other research institutes to be able to conduct full proteomic studies. To that end Dr. Wang has successfully initiated collaboration with two researchers (Drs. Yang Cai and Lizhe Xu) in the Research Institute for Children at Children's Hospital in New Orleans. The research associate, Mr. Qiang Zhang from Dr. Wang's lab, has completed all paper work required by the Children's Hospital in order for him to obtain free access to its proteomic research facilities. The nature of the collaboration is based on the understanding that all publications based on data resulting directly or indirectly from using the instruments at the Research Institute for Children will be jointly written by both parties.

Set up a comprehensive set of 2D gel separation instruments

The following equipment has been purchased, installed, and in operation since the beginning of the research project:

a. BioRad PROTEAN® IEF System with immobilized pH gradients for 2-D
b. Two BioRad Criteion cell for 11-cm gel used as the second-dimension system
c. BioRad PROTEAN®
d. VersaDoc™ Imaging Systems with PDQUEST software

Preliminary results

Using the newly installed two-dimensional gel electrophoresis system, we have developed and optimized working protocols for i) preparation of protein homogenates from cultured breast carcinoma cells; ii) isoelectric focusing of the protein homogenates in an immobilized pH-gradient gel for the first dimension separation, iii) SDS-PAGE second dimension electrophoresis, and iv) gel imaging (see Figure 2 for example 2D gels). Work is underway to identify protein spots that can yield meaningful information on differential protein expression (both qualitative and quantitative) between the MCF-MEK5 and MCF-VEC cell lines. Following gel spot identification, we will move onto experiments involving spot cutting, trypsin digestion, and peptide separation and identification by HPLC-MS/MS.

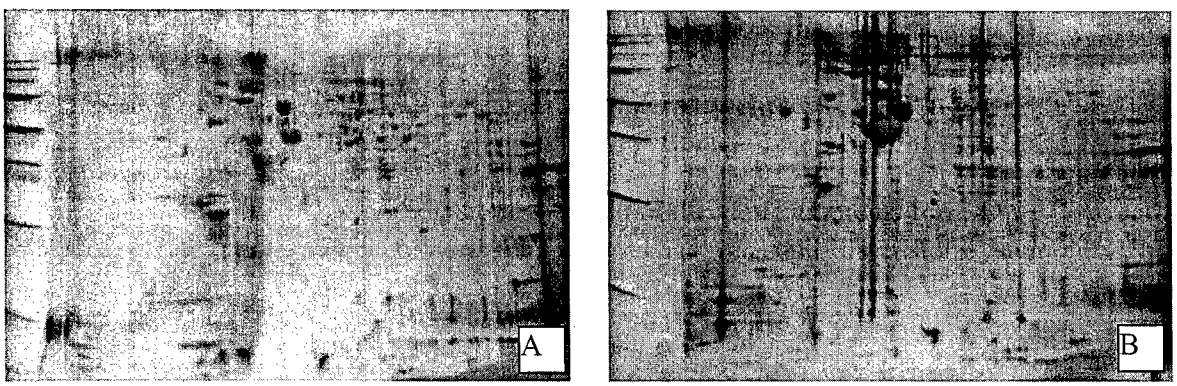

Figure 2. 2D gel electropherogram of protein extracts from (A) MCF-7N-MEK5 cells and (B) MCF-7N-VEC cells using pH 3~10 IPG strips and 11 cm 8~16% linear gradient SDS PAGE gel, and silver stain.

Aim 3: In this task we will use RNA interference strategies to validate a role for the Erk5 pathway in downstream gene expression and in suppression of chemotherapeutic drug-induced apoptosis. Our preliminary analysis revealed survivin expression was increased in drug-resistance and MEK5 expressing breast carcinoma cells. Subsequently we will characterize the role of these downstream targets such as Survivin, in suppression of apoptosis and drug-resistance.

(1) Optimize pSUPER base RNA interference (RNAi) suppression of ERK5 expression in breast carcinoma cells (Month 15-18).
(2) Confirm a role for Erk5 signaling in MCF-7N-CA-MEK5, and MCF-7M-(RESIST) cell survival using pSUPER-Erk5-RNAi. (Months 18-28).
(3) Develop/validate RNAi strategies for Survivin suppression using pSUPER method as above. Use RNAi to implicate Survivin expression in drug resistance and apoptotic signaling of MCF-7 and ZR-75 breast carcinoma cells (Months 24-36).
(4) Develop, validate and use RNAi strategies for novel targets identified from proteomic analysis of drug resistant breast carcinoma cells from Aim 2. (Months 36-48).

Year One Progress

We have further established that shRNA targeting of Erk5 abrogates the ability of MEk5 to enhance tumor growth. We use of RNA interference (RNAi) through either transient transfection of siRNA or through the use of PolII driven RNAi expression constructs to stably ablate/suppress expression of specific genes. Like many molecular inhibition approaches the use of RNAi has its share of problems and can be difficult to effectively use. In our lab we have used siRNA and RNAi-expression constructs to selectively ablate/suppress target genes. In **Figure 3** we demonstrate the use of RNAi expression constructs to generate MCF7 cells stably expressing RNA targeting Erk5. Here we show that MCF7 cells stable expressing Erk5-RNAi demonstrate a downregulation of Erk5 mRNA and protein levels. The ability of MEK5 expression to enhance tumor formation in immunocompromised mice is suppressed by RNAi-mediated ablation of Erk5 expression (**Figure 3C**).

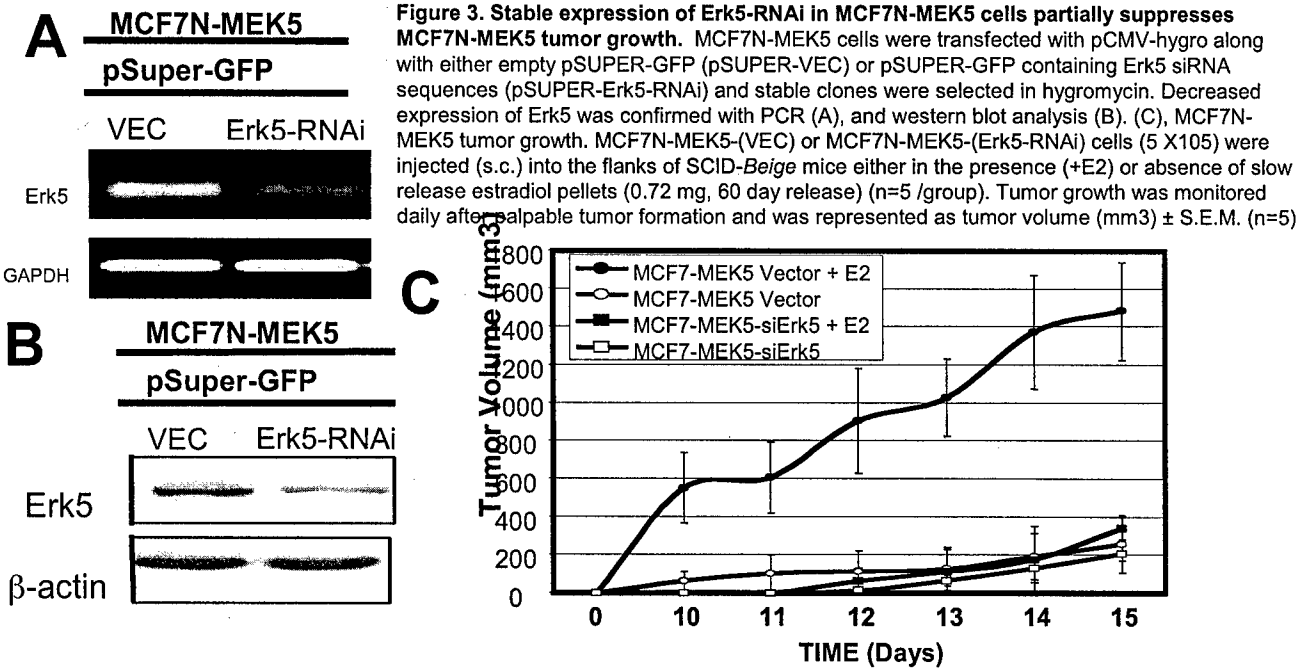

Figure 3. Stable expression of Erk5-RNAi in MCF7N-MEK5 cells partially suppresses MCF7N-MEK5 tumor growth. MCF7N-MEK5 cells were transfected with pCMV-hygro along with either empty pSUPER-GFP (pSUPER-VEC) or pSUPER-GFP containing Erk5 siRNA sequences (pSUPER-Erk5-RNAi) and stable clones were selected in hygromycin. Decreased expression of Erk5 was confirmed with PCR (A), and western blot analysis (B). (C), MCF7N-MEK5 tumor growth. MCF7N-MEK5-(VEC) or MCF7N-MEK5-(Erk5-RNAi) cells (5 X105) were injected (s.c.) into the flanks of SCID-*Beige* mice either in the presence (+E2) or absence of slow release estradiol pellets (0.72 mg, 60 day release) (n=5 /group). Tumor growth was monitored daily after palpable tumor formation and was represented as tumor volume (mm3) ± S.E.M. (n=5)

Project 2

Interactions of estrogen and progestin active environmental chemicals on BC cell proliferation, survival and gene expression

Thomas E. Wiese, Xavier University College of Pharmacy PI (Trainee)
Steven R. Hill, Tulane University School of Medicine (Mentor).

Aim 1: Examine the effects of binary mixtures of estrogen and progestin active environmental compounds on cell proliferation and survival.
(1). Develop treatment mixture matrix and plan for proliferation experiments (Months 1–2).
(2). Perform cell proliferation studies with binary mixtures of pesticides (Months 1–18
(3). Identify mixtures with novel effects on cell proliferation (Months 6–20).

Year One Progress
Research Assistant
The original plans for this project included utilizing the skills of Ms. Suzanne Nehls who is a skilled research assistant in the Wiese lab (since 1999) with 15 years of cell and molecular experience. Ms. Nehls started on the DOD breast cancer project at the beginning of Y1 and along with Dr. Wiese and two students, this core team quickly generated cell proliferation data on pesticide mixtures. However, in June 2004, Dr. Wayne Harris, dean of the Xavier University College of Pharmacy, informed Dr. Wiese that the employment of Ms. Nehls violated the university nepotism rule since she was also married to Dr. Wiese (since 2000). Considering that the dean and university knew about this situation from the start, Dr. Wiese appealed this decision within the university. In July 2004, a termination date for Ms. Nehls was set for September 30 so that Dr. Wiese could advertise, hire and train another research assistant. This initial search was unsuccessful, extended through the fall and still did not produce qualified individuals with any cell culture lab experience. In January 2005, Dr. Wiese hired Ms. Hanh Nguyen, a 2004 graduate from the Xavier Chemistry Department (see resume in Appendix). Ms. Nguyen immediately started training with Dr. Wiese on a daily basis and by February 2005, she was working somewhat independently and producing data with the breast cancer cell proliferation assay. Her solid background in chemistry, biochemistry and molecular biology means that she not only quickly learns lab techniques and processes, but is able to relate experiments to the grant aims and goals. While the process of training Ms. Nguyen requires a very significant amount of time, she is now able to produce meaningful results and gets along well with all in the lab. Dr. Wiese is optimistic that she will be able to learn more techniques in the summer 2005 and within one year, be performing at about optimal capacity for someone of her age and experience. While this change in personnel and the associated training time required was an unexpected setback for the project, the progress is generally on track.

Collaboration between Dr. Wiese at Tulane Cancer Center and Dr. Hill
Dr. Wiese has been in close contact (more than once per week) with Dr. Hill since the start of this project through phone, email or meetings. While the project was designed to take place entirely in the Wiese lab, Dr. Hill has provided input on experimental design and data interpretation. The main contribution of Dr. Hill to this project has been discussions relating to the use of microarray technology to identify specific genes or classes of genes that may be related to the observed mixture effects (see Y1 progress of Aim 2 below). Dr. Hill has also provided insight regarding the management of the overall training program (see tasks 2 and 3 below).

Preliminary results
The series of pesticides included in this study included isomers and metabolites of DDT and methoxychlor. Each are known to have weak estrogen, androgen and/or progesterone activity. A series of MCF-7 proliferation studies were conducted to identify novel interaction effects of binary mixtures of these compounds. The initial studies were designed to include one pesticide at the lowest observed effect level (LOEL) and the other at the highest dose possible (10-5 M). Experiments were also conducted to determine if mixing the pesticide (high dose) with sub-optimal concentrations of estradiol-17β (E2) enhanced estrogen induced proliferation. This series of experiments did not identify mixture combinations with more than the additive cell proliferation activity expected from the compounds alone at the same concentrations. These same mixtures were examined in the MVLN estrogen responsive reporter gene assay where similar additive effects were also observed. At this point, Dr. Wiese decided to examine mixtures that contained one of the

organochlorine pesticides along with one of three organophosphate pesticides. The organophosphates fenitrothion, parathion and methylparathion are known to have no estrogen activity (proliferation or gene induction), but are antagonists for androgen and progesterone receptors. These experiments identified mixtures that did produce breast cancer cell proliferation to a greater extent than would be expected from the sum effect of either pesticide component tested alone. The organophosphates fenitrothion and parathion stimulated the weak estrogen activity of the organochlorines o,p'-DDT, o,p'-DDE, p,p-DDT and p,p'-DDE from 10-40% above the LOEL. That is, concentrations of organochlorines that produce only minimal proliferative responses (<15%), were enhanced to more than 60% with the addition of concentrations of organophosphates that are known to induce minimal (<15%) or no proliferative activity (Figure 4). This observed mixture effect was eliminated by simultaneous antiestrogen treatment (ICI-182,780). The proliferative activity of the methoxychlor metabolite HPTE was also enhanced by co-administration of organophosphates (Figure 4). In an effort to characterize this effect as a stimulation of receptor mediated transactivation, we examined these same organochlorine-organophosphate mixtures in the MVLN estrogen responsive reporter gene assay. No organophosphate enhancement of the weak estrogen activity of the organochlorine pesticides was observed in the reporter gene assay. Thus, we have observed a positive sensitizing or potentiation effect of organophosphate pesticides on the weak estrogen dependant proliferation activity of organochlorine pesticides (increased potency). This action can be eliminated by antiestrogen and is likely estrogen receptor (ER) dependant. The observation that this sensitizing effect was not observed in the reporter gene system suggests that the mechanisms involved are more complex than a simple stimulation of classical ER transactivation activity. Finally, the observation of this sensitizing effect suggests a hypothesis that exposure to low levels of weakly estrogenic pesticides in combination with an organophosphate pesticide might result in more breast cancer cell proliferation than would be expected by the organochlorine alone. The organophosphate compounds in this study are known to have antiandrogen activity. Considering that androgen agonists are known to inhibit estrogen regulated processes in some cells, it is reasonable that treatment with antiandrogens may relieve such supression, resulting in a relative increase in organochlorine induced estrogen activity. The organochlorine compounds in the study are considered persistent contaminants with long elimination half lives. Thus, chronic exposure to low concentrations may have more estrogenic activity than would be expected if cells are sensitized or stimulated by periodic exposure to organophosphate pesticides. Contamination from older pesticides that are no longer used might be more significant if one is exposed to current use pesticides.

Year 2 activities related to Aim 1 will include completing the matrix of pesticide combinations in the proliferation and MVLN reporter gene assays to include all combinations of concentrations as well as experiments that include bisphenol A, an environmental contaminant that has a structure similar to DDT and HPTE. Experiments will also examine of the effects of androgens DHT and hydroxyflutamide (agonist and antagonist), the progestins R5020 and RU486 (agonist and antagonist) as well as organophosphates on cell proliferation induced by sub-optimal concentrations of E2. These experiments will define the range of activity for the sensitization effect and examine effects of the organophosphates on. We may also add a few other pesticides with androgen or progestin activity to explore the hypothesis that any progestins or antiandrogens may either contribute to proliferation or relieve supression of proliferation. Finally, 3-4 mixture combinations that produce the most dramatic sensitization effect in the breast cancer cells will be selected for microarray analysis in Aim 2.

Figure 4 Breast Cancer Cell Proliferation Activity of Pesticide Mixtures

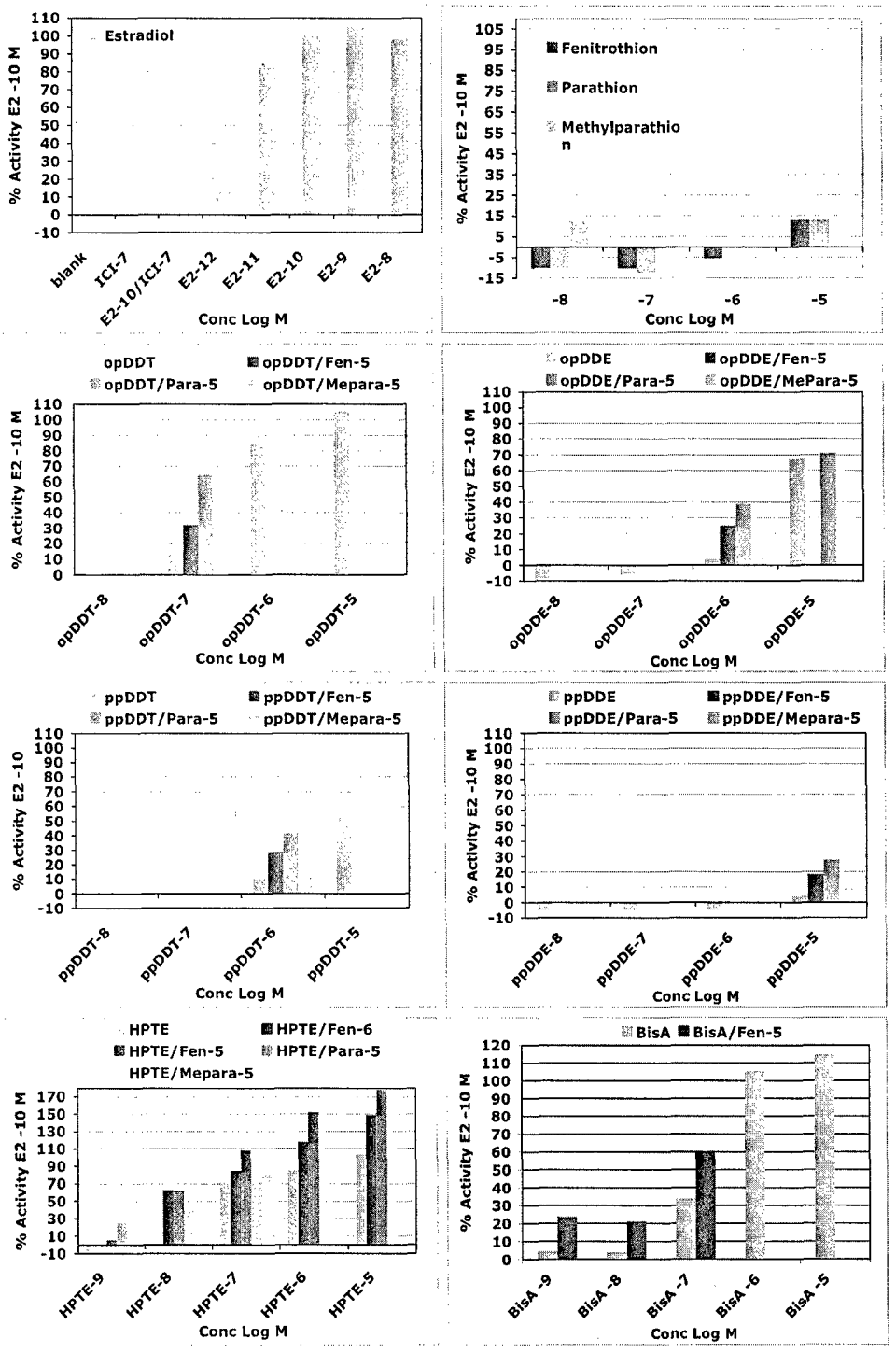

Figure 4 Normalized estrogen activity of pesticides and mixtures from the 7 day MCF-7 proliferation assay. Sub-optimal doses of organochlorines were combined with high does organophosphates (10-5 M) Data shown is average of at least 3 separate 96 well plate experiments with 4 wells/treatment/plate. Positive and negative controls were included on each plate. Concentrations shown are Log M.

Aim 2: Conduct cDNA microarrays to define a set of genes that are coordinately or differentially regulated by treatment with environmental hormones. Preparations from cells grown and exposed to mixtures of hormone active pesticides in the Wiese Lab will be evaluated for differential expression of

genes in the Tulane Center for Gene Therapy.

(1). Identify target genes related to breast cancer cell proliferation from literature searches that will be used in gene array studies (Months 1–12).

(2) Prepare cells for gene array analysis after exposure to mixtures of pesticides. (Months 9–24).

(3) Run gene array analysis on cell preparations and analyze data (Months 12–36).

Year One Progress

We have decided to use focused microarrays such as Superarray rather than the Affymetrix arrays available in the Tulane Cancer Center. This will reduce the cost of the microarray experiments and allow us to focus more on nuclear receptor mechanisms and cancer related genes.

In year 2, Dr. Wiese will have his research assistant Hanh Nguyen trained in microarray methods by working in the Hill lab at the Tulane Cancer Center. She will also go through training courses to at the LCRC core facility to become proficient in the computer based analysis of the microarray results.

Aim 3: Confirm the expression pattern of genes identified by microarray through analysis of gene products (mRNA or protein).

(1) Select 6–10 genes that have been shown by differential display to have novel expression patterns as a result of pesticide mixture treatment (Months 14–36).

(2) Obtain probes for Northern blot analysis of selected genes (Months 14–36).

(3) Perform Northern blots to confirm expression observed in micro array studies (Months 24–48).

(4) Obtain antibodies for Western blot analysis of selected genes (Months 14–36).

(5) Perform Western blots to confirm expression observed in micro array studies (Months 24–48).

Year One Progress

No progress on this aim in year 1.

Deliverables/measurable outcomes:

Drs. Wang and Wiese will prepare or oversee the following:

1. Semiannual reports will be submitted to the PI.

Year One Progress

Even though year one of this project started in April 2004, the award was not received until late April, accounts were not set up at Xavier until June and the Tulane subcontract was not established until July. Thus,Y1 started a bit late and consisted mostly of establishing facilities, gearing up for projects and generating preliminary data. The 6 month progress of each project in the XU-TU DOD Breast Cancer and Prostate Cancer training programs was presented at our first joint meeting in September 2004 (see Task 3 progress below). The two Breast Cancer project reports for the second half of Y1 were submitted to the PI and are included in this Y1 progress report.

2. Students involved in the research will present a poster at the annual research workshop (Months 12, 24, 36, 48).

Year One Progress

In year one, two Xavier undergraduate students have been involved in research activities supporting the breast cancer project in the Wiese lab. Ashley White, a chemistry major and Xavier RISE scholar joined the Wiese lab in May 2004. She immediately learned cell culture methods and then started making progress on breast cancer cell proliferation and reporter gene assays in support of this project as well as another project in the lab that is examining the hormone activity of dietary supplements. Ashley has excellent skills in the lab as well as an aptitude for experimental design and problem solving. In 2004, she decided to start pharmacy school at Xavier beginning fall of 2005 and she has requested to continue her research though the summer of 2005 and during pharmacy school. Ms. White has also expressed interest in a research career after the PharmD program and Dr. Wiese will assist her in presenting at national meetings to provide exposure to non-traditional pharmacy

careers. Uche Obih is a biology major at Xavier who came to the Wiese lab to learn cell culture methods in the summer of 2005. She learned quickly and worked closely with both Ms. Nehls (research assistant) and White to set up and carry out reporter gene assays on pesticide mixtures and dietary supplements. Ms. Obih left the lab as the fall semester started to begin a microbiology research project she planned the year before with another Xavier faculty. Also during this period, Michelle Lang, another undergraduate from the Xavier MARC program finished her second year in the Wiese lab working on the dietary supplement project before graduating in 2005. The situation in the Wiese lab with one research assistant leaving in September followed by a period of some months without a research assistant while searching for a replacement and then hiring a new research assistant in early 2005, did not provide the best environment for training additional students.

Thus, in Y1 of this project, Dr. Wiese focused on generating as much data for Aim 1 as possible with experienced personnel and then on hiring and training a research assistant. He will add more students on the project in Y2. For example, during the spring semester 2005, Dr. Wiese actively recruited P1 and P2 pharmacy students to work on the breast cancer project during summer 2005 and two P1 students expressed interest. Mia Louis and Julie Nguyen will start working part time in the lab in May 2005. They will join Dr. Wiese's new RISE student Hasina Ashe, Biology major, who is going into her junior year in fall 2005. Julie has expressed interest in developing a project that she can build throughout the P2 and P3 years of pharmacy school. Mia has little research experience and will focus on learning basic skills and identifying her area of interest. Dr Wiese will also gain a new student from the Xavier MARC program in August 2005. Both Hasina and the new MARC student are and will be funded by the RISE and MARC programs at Xavier and thus will spend two years doing research in the Wiese lab. Julie and Mia will be funded by the labs dietary supplement project in summer 2005. Then in Fall semester 2005, Julie will be funded by the campus work study program while Mia and Ashley will apply to the Xavier College of Pharmacy Center of Excellence Scholars program for funds to support their research efforts. This approach utilizes the DOD Breast Cancer project to fund students in summer 2005 (Ashley White) while at the same, students will continue working on the DOD project supported by Xavier programs in the 2005-2006 school year. By fall 2005, three pharmacy students and two undergraduate MARC and RISE students will be working in the Wiese lab along with two research assistants (Huiming Li (part time), Hanh Nguyen, one Tulane doctoral student (Kirk Williams) and Dr. Wiese. Some of these students will be working on the Breast Cancer project and some will be working on the dietary supplement project.

In similar form, Dr. Wang focused Y1 on setting up his proteomics equipment and working closely with his research associate to learn 2D gel methods. In Y2, Dr. Wang will involve at least one Xavier student in the proteomics research as well as aspects of the project in the Burow lab at the Tulane Cancer Center.

Both Dr. Wang and Wiese feel that the most effective student training only occurs when the full time members of the lab have sufficient expertise in the methodologies used in the lab. Thus, Y1 in both labs was dedicated to building expertise so that students in Y2 and beyond will have sold faculty and staff mentors from which to learn lab skills.

3. One competitive grant application will be submitted by the end of the funding period.

Year One Progress

Submission of a major equipment proposal to DoD for the acquisition of a tandem mass spectrometer.
In an effort to build up Xavier's capability to conduct independent proteomic research, Dr. Wang submitted a major equipment proposal to DoD's to the Army Research Office for consideration under ARO Broad Agency Announcement W911NF-05-R-0001. The proposal is entitled "High Performance Liquid Chromatography-Tandem Mass Spectrometry for Enhancement of Teaching and Research at Xavier University". The proposal asks for $196,392 for the purchase of an HPLC-MS/MS system. One of the major justifications for the proposal is the ongoing breast cancer research project for which the availability of such an instrument is essential.

Submission of a P20 planning grant to the NCI
A P20 planning grant was developed and submitted to the NCI in Y1. More details are provided in Y1 progress of Task 3 below.

4. Papers will be submitted to peer reviewed journals through the funding period.

Year One Progress
No manuscripts were submitted in Y1.

Training deliverables:

1. The Tulane Cancer Center in conjunction with the Section of Hematology and Medical Oncology and The Cell Signaling group will be directly involved in providing breast cancer research training for Xavier Investigators.

Year One Progress
The support provided from the TCC to each project is described within the progress reports of each project above. In addition, TCC support for the program as a whole is detailed in Task 3 below.

2. Toward the end of the project period, Drs. Wang and Wiese will be Co–PIs in writing an R01 grant in collaboration with Drs. Burow and Hill.

Year One Progress
No R01 collaborative grants are in preparation at this time. We expect that during Y2, the planning for at least one collaborative grant will be started.

Task 2
Assist two Xavier junior faculty to become more competitive in breast cancer research

a. Identify two Junior Faculty with interest in breast cancer research (Month 1).

Year One Progress
In the summer of 2004, Dr. Wiese and Dr. Klassen (coPI of the XU Prostate Training Grant) began identification of XU faculty that were interested in cancer research. This process included meeting with department chairs, junior and senior faculty, and culminated in an email to all XU faculty with information about the opportunities in the DOD Breast and Prostate training programs. Three faculty responded with interest in the Breast Cancer program, Dr Wiese met with each and requested a one page description of research interest and CV so that collaborators in the TCC could identify appropriate TCC faculty to serve a research mentor. This process resulted in one XU chemistry faculty, Dr. David Wolfgang, and one XU biology faculty, Dr. Mary Carmichael, submitting interest statements and CVs. Dr. Wiese then met with Dr. Hill to discuss potential mentors. Dr. Carmichael has been matched with Dr. Asim B. Abdel-Mageed from TCC on a Prostate Cancer project and is now supported by the XU-TU DOD Prostate Cancer program. Dr. Wolfgang has not yet been matched with a TCC mentor and finding a mentor for Dr. Wolfgang is a top priority for summer 2005.

The XU College of Pharmacy has two clinical faculty that have interest in cancer research or women's health. Dr. Susan Hinton has a clinical practice with focus on women's health issues and Dr. Dana Jamero has a clinical practice in oncology. Dr. Jamero was involved in the development of the P20 planning grant to the NCI (see Task 3 below) and her practice is located adjacent to Tulane Medical Center and the TCC. Early in Y2, we plan to more aggressively recruit these individuals to consider developing a project in the Breast Cancer training program. Dr. Wiese has had discussions with the College of Pharmacy administration regarding involvement of pharmacy clinical faculty in the cancer training program. The most reasonable projects would likely involve self diagnosis training at one of the six XU College of Pharmacy out reach clinics for low income minority patients. The TCC director Dr. Weiner has also expressed interest in such programs and has suggested clinical faculty mentors from the TCC.

b. Establish participation of the selected Junior Faculty in Tulane Cancer Center seminars and the weekly signal transduction workshop focused on breast and prostate cancer (Month 2).

Year One Progress
A regular group of XU faculty involved in the DOD Breast and Prostate cancer projects are attending the TCC and LSU CC seminars held most Thursdays at noon. The LCRC signal transduction workshops have not yet started meeting. Dr. Wiese has discussed this situation with Dr. Hill who is in the process or reorganizing these workshops. We expect that the TCC and LCRC cancer focal groups will begin meeting regularly starting in

summer 2005.

c. Determine Tulane Cancer Center mentors for the Junior Faculty and submit a two–page mini proposal for review of the PI and alternate PI (Month 6).

Year One Progress
Preliminary progress has been made in the identification of TCC mentors for the new XU faculty researchers. We expect Dr. Wolfgang to develop a mini-proposal in summer 2005.

d. Junior Faculty collect preliminary data (Months 7–36).

Year One Progress
Progress will be made in this area once faculty are matched with a TCC lab in summer 2005.

e. Junior Faculty develop grant proposal (Months 36–48).

Year One Progress
No Progress in this area in Y1.

Task 3
Establish infrastructure that will create an environment that fosters breast cancer research, in which Xavier faculty will receive substantive training and become more competitive for DoD funding

Year One Progress
When Xavier was awarded the DOD Breast Cancer grant in April 2004, Dr. Rosenzweig, the project PI, announced that she would leave Xavier in May 2004. A plan was formulated where Dr. Wiese, PI of one of the research projects in the Breast Cancer training program would take over program PI responsibilities along with his research project. He would be provided release time for both tasks and be assisted by a part time administrative assistant that would be hired. Dr Wiese served 5 years as a joint faculty between Tulane and Xavier before moving full time to Xavier in 2003. While at Tulane, he became a member of the Tulane Cancer Center and developed a good working relationship with Dr. Steven Hill, Tulane coPI of this project. Dr. Wiese also had also developed a good working relationship with Dr. Klassen, Xavier Chemistry Department, coPI of the XU-YU DOD Prostate Cancer training program, when Dr. Klassen utilized the cell culture facilities in the Wiese lab in 2003-2004.

Soon after the start of the DOD Breast and Prostate grants in Spring 2004, the PI of the DOD Breast Cancer grant (Dr. Wiese) and the coPI of the XU-TU DOD Prostate Cancer grant (Dr. Klassen) started to meet to on a weekly basis to discuss how to combine the resources of these two projects in order to maximize the training goals of both grants. One of the first results of these meetings was that both grants would hold a joint organizational meeting so all involved could discuss how to synergize. Getting all parties together proved challenging and a joint organizational meeting was finally held September 24th in the Xavier College of Pharmacy (see agenda in Appendix). All XU faculty and TU mentors involved in both training programs attended this lunch meeting where overviews and updates of both programs and projects were presented. The main conclusion of this meeting was that we should combine some of the activities of the two training programs to hold a combined yearly symposia was as well as work together as a group to attend Tulane seminars, workshops and other events. We also discussed monthly meetings and decided that current attendance at research group meetings, seminars and workshops were the priority and that meetings of just those involved in one or both of the DOD cancer training programs would be an excessive burden and of little value to the training process. It was also decided that so long as there is good communication between those involved in these programs projects (daily or weekly), formal organizational meetings beyond once a year would be unnecessary. Drs. Klassen and Wiese continued to have biweekly lunch meetings to discuss issues related to both projects throughout Y1 and they plan to continue this practice in Y2. In Y1, we established an email list serve for all Xavier and Tulane faculty involved in both XU DOD cancer training projects and this mechansim has been very helpful for rapid communication of cancer center events, project meetings and organizing car pools to LCRC seminars. We feel that in one year, we have created a program that supports a core group of faculty at Xavier interested in cancer research and we are excited about expanding development of these resources in Y2.

It should be noted that the Tulane Cancer Center is part of the Louisiana Cancer Research Consortium (LCRC) that includes the LSU Cancer Center. The LCRC was devised in 2002, involves significant funding from the

state of Louisiana and will eventually be housed in a new building between the Tulane and LSU medical centers in New Orleans. The LCRC is co-directed by Dr. Roy Weiner (Director of Tulane Cancer Center) and Dr. Oliver Sartor (Director of the LSU Cancer Center). Drs. Klassen and Wiese were invited to the first annual LCRC retreat in January 05. The planning process and meetings that took place at this retreat clearly stated that all Xavier faculty interested in or doing cancer research were welcome to participate in the LCRC through adjunct appointments in Tulane or LSU departments. In addition, Dr. Roy Weiner has keep in close contact with Dr. Wiese regarding the Xavier DOD Breast Cancer training program and has made it clear that he is personally committed to helping Xavier faculty develop cancer research projects and programs. He has opened up all the resources of the Tulane Cancer Center core facilities to Xavier researchers and has invited Xavier faculty to be involved in the Tulane Cancer Centers cancer research symposia held each fall. This Mauvernay Research Excellence Award program includes seminars and posters related to cancer research and concludes with a dinner where TCC faculty meet the invited speakers. Several of the XU faculty involved in the DOD cancer training programs attended the Mauvernay Research Excellence Award program in fall 2004 and Drs. Hill and Weiner made a special effort to introduce the XU faculty to TCC faculty and to the invited speakers. Dr. Weiner also has included clinical faculty from the Xavier College of Pharmacy in ongoing initiatives at the Tulane Cancer Center.

One result of this close relationship between Drs. Weiner and Hill of the TCC and Xavier University is the submission of a P20 planning grant to the NCI in February of 2005 (see Abstract in Appendix). This grant is specifically designed to plan long term collaborations between cancer centers and minority serving institutions. Through a series of meetings starting in October 2004, a P20 grant was developed between the Tulane Cancer Center and Xavier University with Dr. Weiner as the Tulane PI and Dr. Kathleen Kennedy, Associate Dean, Xavier College of Pharmacy as the Xavier PI. At the same time, the PI and co-PI of the Xavier DOD Breast Cancer Training Program, Drs. Wiese and Hill became the P20 grant program managers for each respective institution. Drs Wiese and Hill also took responsibility for the majority of the organization, planning and preparation of this panning grant over a 5 month period leading up to submission in February 2005. The good working relationship of Dr. Wiese and Hill, developed largely from the DOD Breast Cancer Training Program and other prior activities, was critical to working out the complex details of this P20 proposal that involved two very different universities. We feel that the DOD cancer training programs between Tulane and Xavier provided the critical mass required to put together this P20 grant and that the combination of these programs will contribute significantly to the development of self sustaining cancer research programs at Xavier in the future.

The review of the Xavier DOD Breast Cancer Training program requested that an administrative assistant be hired to assist the PI in grant management tasks as well as in planning meetings and coordinating communication between all those involved at XU and TU. In August 2004, Mr. Sergio Alcantera was hired as a part time program manager for this project. Mr. Alcantera came to the Breast Cancer program with 7 years of experience within Xavier as program manager for the Center for Environmental Programs and has a good working relationship with the staff of the XU fiscal office that handles grant and contract funds on campus. Sergio has been a critical component of the BC training program and in addition to planing logistical aspects of meetings, has on many occasions resolved critical situations regarding the financial aspects of the programs accounts and subcontracts. Even though Mr. Alcantera is shared with another program in the college of pharmacy, he is very dedicated to attending to the details of both programs and is always available to resolve problems.

It should be noted that the procurement policies and procedures at XU have been updated and streamlined in 2004 so that purchase orders can be obtained within a few days of request. However, to prevent long delays in the actual ordering process, XU faculty may still have to place the order themselves using the PO number or FAX the PO to the vender. Mr. Alcantera has been very helpful in assisting all those involved in the training project with placing and processing orders.

a. Grant membership in the Tulane Cancer Center to Xavier researchers. Drs. Wang and Wiese will be

granted a status of contributing members and the junior faculty will be granted a status of associate members. Please see attached TCC publication for the definitions (Month 1).

Year One Progress
At this time, only Dr. Wiese has formal membership in the Tulane Cancer Center because he is an adjunct faculty in the Biochemistry Department of the Tulane school of Medicine. Dr. Wang will be granted membership in the cancer center once he is approved as an adjunct in a Tulane department. Dr. Burow (mentor for Dr. Wang) is currently exploring the potential for an adjunct appointment in his home department of Internal Medicine. Cancer center membership for Dr. Wolfgang will occur once he has been matched with a research mentor and receives an adjunct appointment at Tulane.

b. Include Xavier researchers in Tulane Breast Cancer focus group and Journal Club (Months 2).

Year One Progress
The Tulane Cancer Center Focus Groups are now combined with the LSU Cancer center under the LCRC. At the LCRC retreat in January 2005, the following focal groups were established: Molecular Genetics, Molecular Signaling, Immunology, Epidemiology and Clinical Research. To date, while membership in these groups as been established, regular meetings of these groups has not occurred. We plan to hold some of these focal group meetings at Xavier in Y2.

c. Grant access to core research facilities at Tulane Cancer Center (Month 1).

Year One Progress
Access to TCC and LCRC core facilities has been granted to Xavier faculty. These cores include: Genomics, Proteomics, Biostatistics/Bioinformatics, Immunology, and Tissue Acquisition.

d. Include a student in each research project (Month 2 for Drs. Wang and Wiese and Month 8 for the junior faculty).

Year One Progress
See Task 1 above.

e. Establish a monthly brown-bag lunch meeting to bring up research related issues, review proposals and papers, or brainstorm on new directions to improve the cancer program (Month 1).

Year One Progress
Due to the busy schedules of both TCC and XU faculty involved, monthly meetings have proven to be difficult to organize. We have held a number of group and sub group meetings to discuss aspects of individual projects. Many meetings were also held to develop the P20 planning grant. In Y2, we plan to establish a set date for monthly meetings that will coincide with the weekly seminars at the TCC that many faculty from both institutions are going to anyway. We also hope to have mini-program meetings before or after the monthly/bimonthly LCRC focal group meetings.

e. Hold an annual workshop, open to all in the Xavier and Tulane communities and Xavier student body, for all BC participants to present results of the preceding year. Faculty, students, and staff will attend and at least one person from each group will present a talk; students will present posters (Months 12, 24, 36, 48).

A. First workshop titled "Molecular Signaling in Breast Cancer" (Month 12).
B. Second workshop titled "Breast Cancer and the African American Community" (Month 24).
C. Third workshop titled "Funding Opportunities in Breast Cancer Research" (Month 36).
D. Forth workshop titled "Drug Design and Delivery in Breast Cancer" (Month 48).

Year One Progress
Efforts to hold a joint Breast and Prostate symposia in the spring semester 2005 were thwarted by scheduling conflicts within the university. Dr. Wiese and Klassen are now planning on holding the Y1 symposia in the first

or second week of classes of fall semester 2005. We feel that this timing will allow for good student and faculty attendance and also serve as an advertisement for the Breast and Prostate training programs to the whole Xavier community before they get bogged down in the semester. This first symposia will bring in speakers that can directly impact the research projects underway in both training programs and will also include posters from each project. Then, in the spring of 2006, we will hold the Y2 symposia at a time that does not conflict with the various spring activities at Xavier. We will work with the Xavier Festival of Scholars Program in the Fall of 2005 so we can hold our cancer symposia along with the annual Festival of Scholars at Xavier. This way, students presenting at the festival can also participate in the cancer symposia and learn of cancer research opportunities on campus as well as cancer research careers.

f. Subscribe to breast cancer related journals (Month 1).

Year One Progress

After a survey of the cancer research journals available to the Xavier and Tulane communities, we have purchased a subscription to the online journal Breast Cancer Research. In Y2, we will subscribe to the journal Proteomics and the XU-TU Prostate Cancer program will purchase another cancer related journal subscription. Access to Tulane library resources is still limited for XU faculty. Only faculty with adjunct appointments have off campus online access. In Y2 we must establish XU faculty as adjuncts at Tulane to resolve this problem.

Key Research Accomplishments

- We have shown that over expression of MEK5 increases breast cancer tumor volume independent of estrogen.
- We have shown that the combination of organophosphate and organochlorine pesticides can interact to enhance the estrogen activity of the organochlorine.

Reportable Outcomes

1. MCF-7 MEK5 cells that stably express MEK5.
2. Proposal entitled "High Performance Liquid Chromatography-Tandem Mass Spectrometry for Enhancement of Teaching and Research at Xavier University", $196,392, DoD ARO Broad Agency Announcement W911NF-05-R-0001.
3. Proposal entitled "Planning Grant Minority Institution/Cancer Center Collaboration", $703,574, NIH NCI RFA-CA-05-020.

Conclusions

In Y1 of this training program, we have established two collaborative breast cancer research projects and have identified faculty that can develop additional projects in Y2. Most importantly, we have built a framework of activities for XU faculty to utilize for interaction with the TCC to develop cancer research initiatives involving Xavier undergraduate and pharmacy students.

Year Two Synergy and Opportunities

In Y2, we plan to build on established interactions with the XU-TU DOD Prostate Cancer program. Examples of the resulting synergy will be the cancer research symposia, group training activities such as attendance to seminars and TCC focal group meetings, research collaborations and perhaps even sharing TCC mentors that support both the breast and prostate training programs. We also expect to start interaction between XU students involved in both cancer training programs, will encourage student training between the two programs and will include student presentations in the symposia. In Y2, we will also explore the potential for interacting with other HBCUs that have DOD cancer grants to develop a program where students from HBCUs doing cancer research spend a summer at another HBCU institution learning techniques and gaining experience.

Year Two Challenges

The top program priority of Y2 is to establish Dr. Wolfgang and an XU Pharmacy clinical faculty with a TCC mentor to develop a project. The challenge in this process is two fold. Finding the right TCC faculty that is not already overloaded with research and academic responsibilities and then finding the time in the heavily loaded schedule of the clinical faculty so they can develop a project. In Y2 we expect to increase the number of XU students working on the cancer projects. Drs. Wang, Wolfgang and Wiese will pick up MARC and RISE students in the summer and fall semester. Dr. Wolfgang presents a summer program at XU for RISE students where they learn basic molecular techniques. Through this process, he will gain good rapport with the RISE students which should result in an easy transition for the students into research projects. We hope to get XU pharmacy students involved in this program through clinical faculty who develop projects. The two primary research projects of this program must continue to develop capacity for their projects. Dr. Wang will develop a closer interaction with his mentor Dr. Burow through more frequent meetings and focal group research presentations so he can learn more cancer biology and Dr. Burow can learn more about mass spectrometer capabilities. Dr. Wiese must continue training his new research assistant so that his project will stay on schedule. Drs Wiese and Klassen will work closer with the TCC and LCRC in an effort o get the cancer research focal groups and works shops running on a continual basis. We feel this is critical to the success of the training aspects of the program. Release time for research is a problematic issue for XU faculty in the College of Pharmacy. While XU College of Arts and Sciences faculty have a well defined formula where percent effort on a research project translates into reduced teaching load or summer salary (with no teaching), faculty in the college of pharmacy maintain their same teaching load (<50% that of Arts and Sciences faculty) regardless of research funding. Thus, the load for Dr. Wiese was the same in the 2004-2005 academic year as it was in 2003-2004 even though in 2004-2005 he was supported 40% by the DOD Breast Cancer grant for PI and research responsibilities (dedicated 40% of his time). In a normal year, this would not be a problem. In Y1 of this program, Dr. Wiese lost an experienced research assistant and had to search for and train a new person in the lab. This situation with faculty load and release time in the XU College of Pharmacy is also a hinderance for recruiting clinical faculty to develop a cancer research project. The administration of the XU College of Pharmacy is planning to develop a faculty load policy in the near future.

References

NA

Appendices

Curriculum Vitae

Youyuan Jin

Education:

Department of Chemistry, Mississippi State University — Mississippi State, MS
Ph. D. degree, Chemistry — August 1998

California State University, Northridge/Fullerton — Fullerton, CA
Certificate, Chinese Teacher/Scholar Enhancement Program — September 1993

Beijing Foreign Studies University — Beijing, P R. China
Certificate, Advanced English — January 1992

Zhejiang University (formerly Hangzhou University) — Hangzhou, P. R. China
M. S. degree, Chemistry — September 1987

Hangzhou Teachers' College — Hangzhou, P. R. China
B. S. degree, Chemistry — July 1984

Professional Experience:

Organic Vision Inc. — Brossard, QC
Research Scientist — July 2003 - Present

American Dye Sources Inc. — Montreal, QC
Senior Chemist — June 2001 – October 2002

Applied Research Center, Temple-Inland Forest Products Corporation — Diboll, TX
Research Chemist — August 1998 - February 2001

Department of Chemistry, Mississippi State University — Mississippi State, MS
Postdoctoral Fellow. Advisor: Dr. Keith Mead — May 1998 - August 1998

Department of Chemistry, Mississippi State University — Mississippi State, MS
Research assistant. Advisors: Drs. Thomas Fisher and Tor Schultz — August 1993- May 1998

Department of Physics and Chemistry, California State University — Fullerton, CA
Visiting Scholar. Advisor: Dr. Greg Williams — March 1993 - August 1993

Department of Chemistry, California State University — Northridge, CA
Visiting Scholar. Advisor: Dr. Ricardo Silva — October 1992 - March 1993

Department of Chemistry, Hangzhou Educational College — Hangzhou, P. R. China
Assistant and Associate Professor — September 1990 - October 1992

Chemical Research Center, Hangzhou First Pharmaceutical Co. — Hangzhou, P. R. China
Research Chemist — September 1987 – September 1990

Department of Chemistry, Zhejiang University — Hangzhou, P. R. China
Researching assistant. Advisors: Drs. Chen Zhenchu and Peter Stang — September 1984 - October 1987

Research Experience:

Organic Vision Inc. — Brossard, QC
Research Scientist — July 2003 - Present

Separation and synthesis of natural biological compounds; GC-MS, LC-MS, MALDI-TOF MS and tandem mass spectrometry for purification and identification of biological molecules including peptides and proteins.

American Dye Sources Inc. Montreal, QC
Senior Chemist June 2001-October 2002

Design, synthesis, purification, and characterization of various biological dyes. Utilization and maintenance of GC-MS, LC-MS, DSC, Vis-UV-NIR, FTIR, HPLC, GPC

Applied Research Center, Temple-Inland Forest Products Corporation Diboll, TX
Research Chemist August 1998 - February 2001

Separation of natural products by using a variety separation methods including Electrophoresis, HPLC, GC, and ion chromatography, characterization of those compounds by using MS, GC-MS, LC-MS, FTIR and NMR

Department of Chemistry, Mississippi State University Mississippi State, MS
Postdoctoral Fellow May 1998 - August 1998

Synthesis of substituted spiroketals and structure elucidation of those compounds by spectra methods, like GC-MS, LC-MS, FTIR and NMR

Department of Chemistry, Mississippi State University Mississippi State, MS
Research and teaching assistant August 1993- May 1998

Synthesis, characterization, and biological determination of 3-stilbenols and its derivatives as anti-fungi agents; QSAR studies of 3-stilbenols and 4-stilbenols against wood-destroying fungi (Dissertation research)

Department of Physics and Chemistry, California State University Fullerton, CA
Visiting Scholar March 1993 - August 1993

Synthesis and characterization of organochromium compounds by using MS and X-ray electron diffraction

Department of Chemistry, California State University Northridge, CA
Visiting Scholar October 1992 - March 1993

Comparative studies of the science education in the USA and China

Department of Chemistry, Hangzhou Educational College Hangzhou, P. R. China
Assistant and Associate Professor September 1990 - October 1992

Studies on best conditions of Tollens and Fehling reagents used in both hospital and laboratory; Synthesis and purification of intermediates to antibiotic medicines

Hangzhou First Pharmaceutical Company Hangzhou, P. R. China
Research chemist September 1987 - October 1990

Separation, structure elucidation and synthesis of "Yellow Sugar" from a special yellow cane as a sugar substitute for diabetes patients

Department of Chemistry, Zhejiang University Hangzhou, P. R. China
Research assistant September 1984 - October 1987

Studies on polyvalent iodine compounds in organic synthesis; Synthesis of arylated Meldrum's acids; Synthesis of aryl esters of dithiocarbamic acids; Synthesis of aryl arenedithiocarboxylates (Thesis research)

Bibliography:

1. "The Stability of Electro-Opto-Active Organics", Xiao, S.; Jin, Y.; et.al. DMC'03, Taipei, February, **2003**.
2. "Effect of Solvent on Fabrication of Polymeric Light Emitting Devices", Xiao, S.; Jin, Y.; et.al. *Appl. Phys. Lett.*, **2002** (Submitted).
3. "Fungicidal Activities of 3'-Substituted 3-Stilbenols", Jin, Y.; Fisher, T. H.; Schultz, T. P., *Holzforschung*, **2001,** 55, 568.

4. "3-Stilbenols as Potential Fungicidal Agent", Jin, Y., Dissertation, Mississippi State University, **1998**.
5. "Role of Stilbenols in the Natural Durability of Wood: Fungicidal Structure-Activity Relationships", Schultz, T. P.; Hubbard, T. F.; Jin, Y.; Fisher, T. H.; Nicholas, D.D., *Phytochemistry*, **1995**, *34*, 1501.
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8. "The Difference and Similarity In Teacher Training In Hangzhou Institute of Education and California State University, Northridge", Jin, Y., *Essays on Comparative Studies of the Middle School Science Education in the U.S. And China*, **1993**, G1.
9. "The Survey of Chemistry Teachers in Hangzhou Junior High School District", Lu, R.; Jin, Y., *Hangjiaoyuan Xuebao*, **1992**, *2*, 62.
10. "The Lesson of configuration Isomerism", Jin, Y.; Lu, R., *Hangjiaoyuan Xuebao*, **1990**, *4*, 51.
11. "The Progress of Organic Chemistry In China and Western Countries Around the Opium", Jin, Y.; Yu, T.; Yang, X., *Hangjiaoyuan Xuebao*, **1988**, *4*, 23.
12. "How to Avoid False Results When Using Tollen and Fehling Reagents in both Hospital and Laboratory", Jin, Y.; Fan, Q., *Hangjiaoyuan Xuebao*, **1988**, *2*, 53.
13. "Polyvalent Iodine in Synthesis. 3. An Efficient method for the Synthesis of Aryl Arenedithiocarboxylates", Chen, Z.; Jin, Y.; Yang, R., *Synthesis*, **1988**, 723.
14. "Polyvalent Iodine in Synthesis. 2. A New Method for the Preparation of Aryl Esters of Dithiocarbamic Acids", Chen, Z.; Jin, Y.; Stang, P. J., *J. Org. Chem.*, **1987**, *52*, 4117.
15. "Polyvalent Iodine in Synthesis. 1. An Efficient Route to Isopropylidene Arylmalonates (5-Aryl-Substituted Meldrum's Acid)", Chen, Z.; Jin, Y.; Stang, P. J., *J. Org. Chem.*, **1987**, *52*, 4115.

References:

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Dr. Keith Mead
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Dr. Thomas H. Fisher
Professor of Organic Chemistry
Department of Chemistry
Mississippi State, MS 39762
Tel.: 662-325-3584
E-mail: thf1@ra.msstate.edu

HANH MY NGUYEN

OBJECTIVE

To obtain a strong, proficient chemistry background through classroom and laboratory experience in the New Orleans community.

WORK EXPERIENCE

July 2004 XULA, Summer Science Academy N.O., LA

ChemStar Groupleader

- Prepared & instructed module material utilizing my leadership skills.
- Lectured and provided assistance on skill assignments based on individual needs.
- Conducted laboratory exercises by lecturing on chemical concepts, preparing solutions, and presenting demonstrations.

Aug 2003–July 2004 Park Glen Dental Fort Worth, TX

Dental Assistant

- Maintained a clean and safe work environment by preparing and sterilizing dental tools and equipment daily.
- Served as a chair-side assistant during every patient surgery.
- Managed patient relations and served as support personnel.

May 2003-Aug 2003 XULA, Chemistry Dept. N.O., LA

Student Researcher

- Synthesized homogenous, thin film on silicon substrate for application in information technology storage.
- Created thin films by synthesizing solutions using varying concentrations of iron-based compound and application method of spin-coating and annealing.
- Synthesized fine powders from excess solution for characterization through transmission electron microscopy and X-ray diffraction.

May 2002–May 2003 XULA, College of Pharmacy N.O., LA

Student Laboratory Technician

- Trained laboratory rats by feeding, weighing, handling, and administering drugs to them.
- Analyzed vital organs of laboratory rats by reductional analysis.
- Prepared rat brain to test levels of dopamine through high performance liquid chromatography (HPLC).

EDUCATION

July 2001–May 2004 Xavier University of Louisiana New Orleans, LA
B.S., Chemistry/ Biology

Graduated *cum laude.*

COMMUNITY SERVICE & VOLUNTEER

Aug 2002–May 2003 St. Thomas CCD School New Orleans, LA

3rd Grade Teacher

- Guided young students through Bible study to prepare them for their First Communion.
- Prepared lecture and testing materials for the students.
- **Facilitated student-parent involvement in the Vietnamese community.**

Nov.2002, Apr.2003,Oct.2003 Habitat for Humanity New Orleans, LA

Volunteer Worker

- Assisted low-income families to build their new homes.
- Served by painting the walls and ceilings.
- **Also served by installing vinyl sidings and interior trim.**

Nov.2002–Dec.2002 Tulane School of Medicine New Orleans, LA

Research Project: "Gambling Patterns Among Asian-American Youth" Participant

- Helped administer surveys to Asian American youths in order to retrieve public data used so that the right private and public resources would be committed to address intervention and treatment needs of pathological gamblers within the Asian-American community.

Sept. 2002 LA Office of Public Health-Dept.of Health & Hospital N.O., LA

Focus Group Participant

- **Recruited and organized students to participate in a focus group in order to discuss the growing problem of smoking within the Vietnamese community.**

EXTRACURRICULAR ACTIVITIES

- .Member of Cultural Unity Club, Biology Club, & Xavier University Asian Association (XUAA).
- **.Dance Coordinator for XUAA and Mary Queen of Vietnam Church.**

PROFESSIONAL MEMBERSHIP & AWARDS RECEIVED

- Phi Lambda Upsilon National Honorary Chemical Society, Beta XI Chapter.
- Dean's List.
- **Louisiana TOPS Opportunity Award.**

SERGIO R. ALCANTARA, JR.

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EDUCATION

Nov 17 – 21, 1997 CompUSA Computer Training New Orleans, LA
Course on Microsoft NT Server 4.0 System Architecture

Oct 27 – 28, 1997 CompUSA Computer Training New Orleans, LA
Course on System Administration for Microsoft NT Server 4.0

Dec 30, 1996- Jan 10, 1997 John C. Stennis Space Center, MS
National Aeronautics Space Administration
Seminar/Workshop on Introduction to Geographic Information System and Image Processing Techniques for the Classification of Remotely Sensed Imagery

1979 Mapua Institute of Technology Manila, Philippines
B. S. in Environmental and Sanitary Engineering

1978 Mapua Institute of Technology Manila, Philippines
B. S. in Civil Engineering

1970 Luis Bernardo Memo. High School Laguna, Philippines
High School Diploma

PROFESSIONAL EXPERIENCE

August 24, 2004 – Present Xavier University of LA New Orleans, LA
Grant Specialist
College of Pharmacy – Division of Basic Pharmaceutical Sciences

- Interpret funding agency guidelines for proposal submissions, and responses to Requests for Proposal
- Provide grant and budget advise to the principal investigator in preparation for proposals to federal, state and some private funding agencies
- Review proposal formats to ensure adherence to funding agency guidelines (e.g. page limitations, type-size, required contents, etc.)
- Develop and review grant budgets including consolidated budgets for compliance with funding agency and university policies and guidelines
- Interpret and implement regulations governing expenditures and award administration for federal, state and private funding agencies
- Review all award agreements to ensure that terms and conditions are acceptable and in compliance with institution policies (e.g. publishing rights, intellectual property rights, etc.)
- Ensure grant compliance and reporting with all funding agency during implementation.
- Review all salary, subcontractor and equipment charges to grants and contracts to ensure that they are allowable under the terms and conditions set forth by the funding agency

- Review records pertaining to material assets to ensure that they are properly procured, maintained safeguarded and recorded.
- Implement grant tracking/monitoring system with the university SCT Banner and Brio
- Ensure monthly financial reports, grant reports, and reconciliation with SCT Banner and Brio
- Coordinate operational plan impact on existing grant structure, advise on action to be taken
- Monitor grant expenditures and alert the principal investigator of any unauthorized expenses
- Monitor daily and monthly activity of grant budgets
- Advise the principal investigator on all financial matters including any expenditure variances against budgets and other major deficiencies and ensure that corrective action is taken.
- Facilitate, process and review requisitions and accounting entries into SCT Banner
- Review invoices as to its accuracy for approval by the principal investigator for payment
- Ensure proper charging of expenses with proper supporting documentation for all payments and other accounting entries.
- Produce monthly financial statements, preparation of supporting schedules and spreadsheets.
- Meet periodically with principal investigator to review grant reports
- Prepare regular internal accounting reports for management decision-making tool.
- Monitor grants status, revisions, new grant agreements, grant termination, reporting, etc.
- Ensure that all activities are reflected in program deliverables and achievement of contractual benchmarks
- Coordinate with the university Fiscal Service Department on all matters in relation to the grant's financial status , budgets and procurements
- Planning and organizing meetings and workshops related to the grant
- Provide administrative support to principal investigators

Jan 12, 2004 – May 31, 2004 **Xavier University of LA** **New Orleans, LA**
Program Assistant
Center for Environmental Programs (CEP)

- Network administrator of the department's local area network (LAN);
- Maintain and upgrade computers and other related equipment to its good and reliable working condition. Build new computers to meet the demands of new technology;
- Develop and maintain the database of the department's inventory of equipment, furniture, software and literature;
- Maintain the Paradox database for the Consortium for Environmental Risk Evaluation (CERE) project;
- Provide technical support for training, workshop and other related activities sponsored by CEP;
- Provide technical assistance in Geographic Information System (GIS) and related software and hardware to CEP Researchers and student workers;
- Keep track of the budget and expenditures of all CEP Grants using Banner Web;
- Prepare requisitions to purchase equipment, furniture, office supplies for the department's operational needs using Banner Web;
- Review and approved the department's employees and student workers time sheets using KRONOS Workforce Central as to its accuracy prior to submission for payroll;
- Assist in the preparation of reports for the department;
- Any other tasks that the Director for CEP assigned from time to time.

Feb 1, 2002 – Jan 11, 2004 Xavier University of LA New Orleans, LA
Program Manager
Center for Environmental Programs (CEP)

- Network administrator of the department's local area network (LAN);
- Maintain and upgrade computers and other related equipment to its good and reliable working condition. Build new computers to meet the demands of new technology;
- Develop and maintain the database of the department's inventory of equipment, furniture, software and literature;
- Maintain the Paradox database for the Consortium for Environmental Risk Evaluation (CERE) project;
- Provide technical support for Geographic Information System (GIS) training, workshop and other related activities sponsored by CEP-GIS Lab;
- Provide technical assistance in GIS and related software and hardware to CEP Researchers and student workers;
- Keep track of the budget and expenditures of all CEP Grants using Banner Web;
- Prepare requisitions to purchase equipment, furniture, office supplies for the department's operational needs;
- Review the department's employee time sheets as to its accuracy prior to submission for payroll;
- Assist in the preparation of reports for the department;
- Maintain and oversee the day to day operation of the department;
- Prepare Personnel Action forms for new and current employees;
- Any other tasks that the Director for CEP assigned from time to time.

June 1, 1997 – Jan 31, 2002 Xavier University of LA New Orleans, LA
Research Associate
Center for Environmental Programs (CEP)

- Provide technical support for Geographic Information System (GIS) training and workshop and related activities sponsored by the department/GIS lab;
- Develop and maintain a data base to keep control of circulation of the GIS lab equipment, software, and literature;
- Provide technical assistance in GIS and related software to the department's researchers;
- Serves as systems administrator of the department's local area network (LAN);
- Keep track of the budget and expenditures of all CEP Grants using Banner Web;
- Prepare requisitions to purchase equipment, furniture, office supplies for the department's operational needs;
- Review the department's employee time sheets as to its accuracy prior to submission for payroll;
- Assist in the preparation of reports for the department;
- Any other tasks that the Director for CEP assigned from time to time.

May 1993- April 1996 North American Auto Export Tampa, FL
Office Manager

- Responsible for the day-to-day operation of the office which includes bookkeeping and preparation of documents necessary for shipping of cars for export.

Apr 1980 - Dec 1991 Home Insurance & Guaranty Corp. Manila, Phil.
Division Head
Project Management Group of Acquired Assets Department

- Responsible for the rehabilitation and maintenance of 1,400 acquired housing units (located all over the country under the government finance housing programs;
- Responsible for the disposition of the said housing units thru bidding or negotiated sale;
- Responsible for the leasing/renting of said housing units if there are no takers/buyers;
- Responsible for facilitating housing loans in coordination with different banks and financing institutions;
- Responsible for the determination of sale/rental prices of the units available for disposition;
- Responsible in the restructuring of old housing loans, if necessary;
- Responsible for the implementation of the Secondary Mortgage Market System under the National Shelter Program of the Housing and Urban Development Coordination Council (HUDCC).

Aug 1979 - Mar 1980Farm Systems Development Corp. Manila, Phil.
Project Manager
Engineering Department

- Responsible for the development and construction of government financed housing projects in the Island of Mindanao, Philippines.

Oct 1978 - July 1979 Construction & Dev. Corp. of the Phil. Manila, Phil.
Civil Engineer
Process Plant Department

- Responsible for the installation and maintenance of processing plants (batching, asphalt, crusher).

July 1974 - Aug 1976 Banco Filipino Homes Dev. Corp. Manila, Phil.
Assistant Technical Supervisor

- Responsible for the development, construction and maintenance of housing units and a resort hotel in BF Homes Subdivision, Paranaque, Manila, Philippines.

COMPUTER SKILLS

- **Proficient in Windows Operating System (i.e. 95, 98, XP, 2000, NT workstation), Microsoft Office 95/97/2000 (i.e. Word, Excel, PowerPoint, Access, Publisher), Photoshop, Acrobat Writer, Paradox Database and most popular computer software.**
- **Proficient in system administration of Microsoft NT Server 4.0 and Win 2000.**

GEOGRAPHIC INFORMATION SYSTEM

- **Command of OSU-MAP, Arcview 2.1 and 3.0, and ArcInfo 7.0.**
- **Basic knowledge of ERDAS Imagine and Envi.**

AFFILIATION IN COMMUNITY ORGANIZATION

- **Active member of St. Jerome Parish Church**
- **Active member of PTO of Bonnabel High School**

LANGUAGE ABILITY

- **Write, read and speak fluently in English.**
- **Write, read and speak fluently in Pilipino.**

REFERENCES

- **Dr. Thomas Wiese**
  Assistant Professor, Biochemistry and Principal Investigator Division of Basic Pharmaceutical Sciences, College of Pharmacy Xavier University of Louisiana (504) 520-7433

- **Dr. Howard Mielke**
  Professor and Principal Investigator
  Division of Basic Pharmaceutical Sciences, College of Pharmacy Xavier University of Louisiana (504) 520-7523
- **Ms. Joyce Sandifer**
  Director, Fiscal Operations
  Xavier University of Louisiana (504) 520-5230

Form Approved Through 09/30/2007 OMB No. 0925-0001

Department of Health and Human Services
Public Health Services

Grant Application

Do not exceed character length restrictions indicated.

LEAVE BLANK—FOR PHS USE ONLY.

Type	Activity	Number
Review Group		Formerly
Council/Board (Month, Year)		Date Received

1. TITLE OF PROJECT *(Do not exceed 81 characters, including spaces and punctuation.)*
Planning Grant Minority Institution/Cancer Center Collaboration

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION ☐ NO ☐ YES
(If "Yes," state number and title)
Number: CA-05-020 Title: Planning Grant Minority Institution/Cancer Center Collaboration

3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR — **New Investigator** ☐ No ☒ Yes

3a. NAME (Last, first, middle)
Kennedy, Kathleen B

3b. DEGREE(S)
Pharm.D.

3h. eRA Commons User Name

3c. POSITION TITLE
Associate Professor of Clinical Pharmacy, Associate Dean

3d. MAILING ADDRESS *(Street, city, state, zip code)*

3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT
Division of Clinical and Administrative Sciences

3f. MAJOR SUBDIVISION
College of Pharmacy

3g. TELEPHONE AND FAX *(Area code, number and extension)*
TEL: 504 520-7426 FAX: 504 520-7954

E-MAIL ADDRESS:
kkenned1@xula.edu

4. HUMAN SUBJECTS RESEARCH ☒ No ☐ Yes

4b. Human Subjects Assurance No.

4c. Clinical Trial ☐ No ☐ Yes

4d. NIH-defined Phase III Clinical Trial ☐ No ☐ Yes

4a. Research Exempt ☐ No ☐ Yes

If "Yes," Exemption No.

5. VERTEBRATE ANIMALS ☒ No ☐ Yes

5a. If "Yes," IACUC approval Date

5b. Animal welfare assurance no.

6. DATES OF PROPOSED PERIOD OF SUPPORT *(month, day, year—MM/DD/YY)*		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT	
From	Through	7a. Direct Costs ($)	7b. Total Costs ($)	8a. Direct Costs ($)	8b. Total Costs ($)
12/01/05	11/30/09				

9. APPLICANT ORGANIZATION
Name Xavier University of Louisiana
Address 1 Drexel Drive
New Orleans, LA 70125-1098

10. TYPE OF ORGANIZATION
Public: → ☐ Federal ☐ State ☐ Local
Private: → ☒ Private Nonprofit
For-profit: → ☐ General ☐ Small Business
☐ Woman-owned ☐ Socially and Economically Disadvantaged

11. ENTITY IDENTIFICATION NUMBER
72-0635884
DUNS NO. 02-085-7876 Cong. District 02

12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE
Name Gene D'Amour
Title Senior Vice President for Resource Development
Address Xavier University of Louisiana
1 Drexel Drive
New Orleans, LA 70125-1098
Tel: (504)520-5444 FAX: (504) 520-7901
E-Mail: gdamour@xula.edu

13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Name Calvin S. Tregre
Title Senior Vice President for Administration
Address Xavier University of Louisiana
1 Drexel Drive
New Orleans, LA 70125-1098
Tel: (504) 520-7539 FAX: (504) 520-7586
E-Mail: ctregre@xula.edu

14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.	SIGNATURE OF PI/PD NAMED IN 3a. *(In ink. "Per" signature not acceptable.)*	DATE 02/21/05
15. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.	SIGNATURE OF OFFICIAL NAMED IN 13. *(In ink. "Per" signature not acceptable.)*	DATE 02/21/05

DESCRIPTION: See instructions. State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project (i.e., relevance to the **mission of the agency**). Describe concisely the research design and methods for achieving these goals. Describe the rationale and techniques you will use to pursue these goals.

In addition, in two or three sentences, describe in plain, lay language the relevance of this research to **public** health. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. **DO NOT EXCEED THE SPACE PROVIDED.**

The Xavier University of Louisiana at New Orleans (XULA) and the Tulane Cancer Center (TCC) of Tulane University Health Sciences Center propose to develop an effective, sustainable, and mutually beneficial partnership in cancer research and education that focuses on African-American cancer disparities. This application focuses on planning and developing a Partnership by building on complementary institutional strengths conducting joint planning in cancer research and cancer education. The partnership will plan, prioritize, and implement a series of linked pilot initiatives that will lead toward the development of significant collaborative competitive research projects and educational programs aimed at faculty, fellows, and students. Specific collaborative components of the proposal include: pilot research projects; pilot education programs to mentor students in cancer research as well as provide cancer education (courses in Cancer Biology, Cultural Sensitivity and Diversity). This process will enhance the career development for faculty and students resource and provide infrastructure enhancement. XULA offers the partnership: 1) a reputation for providing high quality educational experiences that launch African American students into careers in medicine, biomedical research and pharmacy; 2) a cluster of faculty and students interested in cancer research collaborations and training programs; 3) an established Institute for Minority Health and Health Disparity Research and Education. The TCC and Tulane University bring to the Partnership: 1) extensive experience and expertise in basic science and clinical cancer research; 2) collaborative and training opportunities in cancer research for faculty from XULA; 3) equipment and cores for the effective accomplishment of research projects; and 4) cancer research training and educational opportunities for students interested in careers in cancer research. These complementary institutional strengths will help the partnership: 1) establish an effective cancer research infrastructure/program and increase training of faculty and students from a minority serving institution; and 2) enhance student, trainee, and faculty cancer education emphasizing cancer-related disparities in pathogenesis, prevention and outcome, and increase the training and sensitivity of students and scientists at XULA and the TCC to the challenges and opportunities in studying and addressing cancer research in the context of health disparity.

PERFORMANCE SITE(S) (organization, city, state)

Xavier University of Louisiana
1 Drexel Drive
New Orleans, LA 70125

Tulane Cancer Center
Tulane University Health Science Center
1430 Tulane Avenue
New Orleans, LA 70112

Principal Investigator/Program Director (Last, First, Middle): Kennedy, Kathleen B

KEY PERSONNEL. See instructions. *Use continuation pages as needed* to provide the required information in the format shown below. Start with Principal Investigator. List all other key personnel in alphabetical order, last name first.

Name	eRA Commons User Name	Organization	Role on Project
Kennedy, Kathleen B		Xavier Univ. of Louisiana	Principal Investigator
Wiese, Thomas		Xavier Univ. of Louisiana	XULA-Prog. Manager

OTHER SIGNIFICANT CONTRIBUTORS

Name	Organization	Role on Project
Blake, Robert	Xavier Univ. of Louisiana	Internal Advis. Comm.
Dieninger, Prescott	Tulane University	Internal Advis. Comm.
Hill, Steven, M.	Tulane University	MSI- Program Manager
Weiner, Roy	Tulane University	Co-Principal Investigator

Human Embryonic Stem Cells ☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://stemcells.nih.gov/registry/index.asp. *Use continuation pages as needed.*

If a specific line cannot be referenced at this time, include a statement that one from the Registry will be used.

Cell Line

Disclosure Permission Statement. Applicable to SBIR/STTR Only. See SBIR/STTR instructions. ☐ Yes ☐ No